

**TRANSLATION**

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>05-F-003PCT</b>	<b>FOR FURTHER ACTION</b>	See Form PCT/IPEA/416
International application No. <b>PCT/JP2005/001991</b>	International filing date ( <i>day/month/year</i> ) <b>03.02.2005</b>	Priority date ( <i>day/month/year</i> ) <b>10.02.2004</b>
International Patent Classification (IPC) or national classification and IPC <b>C12N15/09 (2006.01) , C12N1/15 (2006.01) , C12N1/19 (2006.01) , C12N1/21 (2006.01) , C12N5/10 (2006.01)</b>		
Applicant <b>JAPAN SCIENCE AND TECHNOLOGY AGENCY</b>		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items: <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2005/001991

## Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☒ the international application as originally filed/furnished
- ☐ the description:
- pages \_\_\_\_\_ as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the claims:
- nos. \_\_\_\_\_ as originally filed/furnished
- nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the drawings:
- sheets \_\_\_\_\_ as originally filed/furnished
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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## Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 8-11

because:

☒ the said international application, or the said claims Nos. 10-11  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

Claims 10 to 11 pertain to methods for the treatment of the human body by means of therapy, and thus relate to a subject matter which this International Searching Authority is not required to carry out a search under the provisions of Article 34(4) (a) (i) of the PCT and Rule 67.1 (iv) of the Regulations under the PCT.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_  
are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 8-9 [Refer to the Supplemental Box] are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 8-11

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	2, 3	YES
	Claims	1, 4-7	NO
Inventive step (IS)	Claims	2, 3	YES
	Claims	1, 4-7	NO
Industrial applicability (IA)	Claims	1-7	YES
	Claims		NO
2. Citations and explanations (Rule 70.7)			
Document 1: US 6010908 A (The Regents of the University of California), 04 January 2000			
Document 2: US 2002/0160514 A1 (Kaarin Kerr GONCZ), 31 October 2002			
Document 3: GONCZ et al., "Targeted replacement of normal and mutant CFTR sequences in human airway epithelial cells using DNA fragments," Hum. Mol. Genet., 1998, Vol. 7, No. 12, pages 1913 to 1919			
Document 4: COLOSIMO et al., "Targeted correction of a defective selectable marker gene in human epithelial cells by small DNA fragments," Mol. Ther., February 2001, Vol. 3, No. 2, pages 178 to 185			
Document 5: LING and ROBINSON, "Approaches to DNA Mutagenesis: An Overview," Anal. Biochem., 1997, Vol. 254, pages 157 to 178			
Document 6: GRUENERT et al., "Sequence-specific modification of genomic DNA by small DNA fragments," J. Clin. Invest., September 2003, Vol. 112, No. 5, pages 637 to 641			
Document 7: KOWALCZYKOWSKI, "Initiation of genetic recombination and recombination-dependent			

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

replication, Trends Biochem. Sci., April  
2000, Vol. 25, pages 156 to 165

Claims 1 and 4 to 7

The inventions set forth in claims 1 and 4 to 7 lack novelty and do not involve an inventive step in the light of document 1 cited in the international search report.

Document 1 discloses a method for modifying the nucleic acids of a DNA sequence, wherein a 491 base pair single-stranded DNA fragment that was created from a plasmid by means of a PCR amplification technique is introduced into the interior of a cell, and also discloses cells and organisms wherein nucleic acids have been modified by means of the abovementioned method (refer to columns 7 to 12, and to examples 11, 18 and 19). Although document 1 does not specifically indicate that the single-stranded DNA fragment was prepared from single-stranded DNA, the double-stranded DNA that constitutes the abovementioned plasmid is transformed into single-stranded DNA during the thermal denaturation step of the PCR method; therefore, the abovementioned 491 base pair single stranded DNA fragment can be considered to have been prepared from single stranded DNA.

However, the abovementioned finding does not apply to the configurations of the invention set forth in claim 1 which include a step wherein the single stranded DNA fragment is cleaved as opposed to being prepared.

Claims 2 and 3

The inventions set forth in claims 2 and 3 are novel and involve an inventive step in relation to

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

document 1 and documents 2 to 7, which are cited in the international search report.

That is to say, the technique for introducing a single stranded DNA fragment that lacks a complimentary strand into a cell, wherein a single stranded DNA fragment is cleaved from "phagemid DNA" and the single stranded DNA fragment is homologous to the "sense chain" of the target DNA sequence, is not disclosed in any of documents 1 to 7. On the other hand, the inventions in question exhibit a significant effect in that the use of a single stranded DNA fragment improves the efficiency with which it is possible to modify the nucleic acids of a target DNA sequence.

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## Supplemental Box Relating to Sequence Listing

## Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
- a. type of material
- ☒ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☐ in written format
- ☒ in computer readable form
- c. time of filing/furnishing
- ☐ contained in the international application as filed
- ☒ filed together with the international application in computer readable form
- ☐ furnished subsequently to this Authority for the purposes of search and/or examination
- ☐ received by this Authority as an amendment\* on \_\_\_\_\_
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

\* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box III

With regards to the inventions set forth in claims 8 and 9, which are intended to be used as therapeutic medicaments, the present application does not provide sufficient support in the form of pharmacological data or the like to demonstrate that it is actually possible to use said inventions as therapeutic medicaments, even with consideration of the examples and the like therein; therefore, it is not considered to be possible to use any 300 to 3000 base single-stranded DNA fragment that was prepared from a single-stranded DNA as a therapeutic medicament, even with consideration of common technical knowledge at the time the present application was filed.